Amendments to the Claims

The listing of claims will replace all prior versions, and listings of claims in the application.

Claims 1-166 (Canceled).

Claim 167 (Currently Amended). A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising:

(a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides;

(b) glycoengineering said host cell, wherein said glycoengineering comprises genetically manipulating said host cell so that said host cell has a decreased level of activity of at least one glycoprotein-modifying glycosyltransferase;

(c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and

(d) isolating said recombinant antibody;

wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered.

Claim 168 (Previously presented). The method of claim 167, wherein said antibody has increased Fc-mediated cellular cytotoxicity.

Claim 169 (Previously presented). The method of claim 167, wherein said antibody has increased Fc receptor binding affinity.

Claim 170 (Currently amended). A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising:

(a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides;

(b) glycoengineering said host cell, wherein said glycoengineering comprises genetically manipulating said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltransferase selected from the group consisting of: β(1,4)-N-acetylglucosaminyltransferase III and α-mannosidase II;

(c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and

(d) isolating said recombinant antibody;

wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered.

Claim 171 (Previously presented). The method of claim 170, wherein said antibody has increased Fc-mediated cellular cytotoxicity.

Claim 172 (Previously presented). The method of claim 170, wherein said antibody has increased Fc receptor binding affinity.

Claim 173 (Previously presented). The method of claim 171 or 172, wherein said glycoprotein-modifying glycosyltransferase is β(1,4)-N-acetylglucosaminyltransferase III.

Claim 174 (Previously presented). The method of claim 173, wherein expression of said β(1,4)-N-acetylglucosaminyltransferase III is increased.

Claim 175 (Previously presented). The method of claim 171 or 172, wherein said glycoprotein-modifying glycosyltransferase is α-mannosidase II.

Claim 176 (Previously presented). The method of claim 175, wherein expression of said α-mannosidase II is increased.

Claim 177 (Previously presented). The method of claim 173, wherein said host cell also has an altered level of activity of α-mannosidase II.

Claim 178 (Previously presented). The method of claim 177, wherein expression of both said β(1,4)-N-acetylglucosaminyltransferase III and said α-mannosidase II is increased.

Claim 179 (Previously presented). The method of claim 177, further comprising glycoengineering said host cell so that said host cell has an altered level of activity of β(1,4)-galactosyltransferase.

Claim 180 (Previously presented). The method of claim 171 or 172, wherein said glycoengineering comprises introducing into said host cell at least one polynucleotide encoding an exogenous glycoprotein-modifying glycosyl transferase selected from the group consisting of β(1,4)-N-acetylglucosaminyltransferase III and α-mannosidase II.

Claim 181 (Previously presented). The method of claim 180, wherein said exogenous glycoprotein-modifying glycosyl transferase is β(1,4)-N-acetylglucosaminyltransferase III.

Claim 182 (Previously presented). The method of claim 180, wherein said exogenous glycoprotein-modifying glycosyl transferase is α-mannosidase II.

Claim 183 (Previously presented). The method of claim 181, further comprising introducing into said host cell a polynucleotide encoding α-mannosidase II.

Claim 184 (Previously presented). A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising:

(a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides;

(b) glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltransferase;

(c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and

(d) isolating said recombinant antibody;

wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein the predominant N-linked oligosaccharide in the Fc region of said antibody produced by said glycoengineered host cell is not a high-mannose structure.

Claim 185 (Currently amended). The method of claim 184, wherein <u>said</u> antibody has increased Fc-mediated cellular cytotoxicity.

Claim 186 (Currently amended). The method of claim 184, wherein <u>said</u> antibody has increased Fc receptor binding affinity.

Claim 187 (Previously presented). The method of claim 185 or 186, wherein said antibody is a therapeutic monoclonal antibody having a human Fc region and that selectively binds an antigen expressed by cancer cells, and wherein the majority of oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are nonfucosylated.

Claim 188 (Previously presented). A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising:

(a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides;

(b) glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltransferase;

(c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and

(d) isolating said recombinant antibody;

wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein the Fc region containing N-linked oligosaccharides in said antibody further comprises an increased proportion of GlcNAc residues compared to the corresponding antibody produced by the same host cell that has not been glycoengineered.

Claim 189 (Currently amended). The method of claim 188, wherein <u>said</u> antibody has increased Fc-mediated cellular cytotoxicity.

Claim 190 (Currently amended). The method of claim 188, wherein said antibody has increased Fc receptor binding affinity.

Claim 191 (Currently amended). A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising:

(a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides;

(b) glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltransferase;

(c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and

(d) isolating said recombinant antibody;

wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein said antibody produced by said glycoengineered host cell has an increased proportion of GlcNAc residues in the Fc region relative to the proportion of fucose residues compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein said antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity as a result of said glycoengineering.

Claim 192 (Previously presented). The method of claim 191, wherein said antibody has increased Fc-mediated cellular cytotoxicity.

Claim 193 (Previously presented). The method of claim 191, wherein said antibody has increased Fc receptor binding affinity

Claim 194 (Previously presented). The method of claim 192 or 193, wherein said GlcNAc residues are bisecting.

Claim 195 (Previously presented). The method of claim 194, wherein said GlcNAc residues are bisecting and wherein said bisected oligosaccharides are of hybrid type.

Claim 196 (Previously presented). The method of claim 194, wherein said GlcNAc residues are bisecting and wherein said bisected oligosaccharides are of complex type.

Claim 197 (Currently amended). A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising:

(a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides;

(b) glycoengineering said host cell, wherein said glycoengineering comprises genetically manipulating said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltranferase;

(c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and

(d) isolating said recombinant antibody;

wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding

antibody produced by the same host cell that has not been glycoengineered, and wherein said recombinant antibody produced by said glycoengineered host cell exhibits at least an 80% increase in maximal ADCC activity compared to the same antibody produced by the same host cell under identical culture and purification conditions, but which has not been glycoengineered.

Claim 198 (Currently amended). The method of claim 197, wherein said antibody has increased Fc-mediated cellular cytotoxicity.

Claim 199 (Currently amended). The method of claim 197, wherein said antibody has increased Fc receptor binding affinity.

Claim 200 (Currently amended). A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising:

(a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides;

(b) glycoengineering said host cell, wherein said glycoengineering comprises genetically manipulating said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltranferase;

(c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and

(d) isolating said recombinant antibody;

wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein

said recombinant antibody has an increased proportion of nonfucosylated oligosaccharides in the Fc region as a result of said glycoengineering compared to the corresponding antibody produced by the same host cell that has not been glycoengineered.

Claim 201 (Currently amended). The method of claim 200, wherein said antibody has increased Fc-mediated cellular cytotoxicity.

Claim 202 (Currently amended). The method of claim 200, wherein said antibody has increased Fc receptor binding affinity.

Claim 203 (Previously presented). A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising:

(a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides;

(b) glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltranferase;

(c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and

(d) isolating said recombinant antibody;

wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein the predominant N-linked oligosaccharide in the Fc region of the antibody produced by said glycoengineered host cell is nonfucosylated.

Claim 204 (Previously presented). The method of claim 203, wherein said antibody has increased Fc-mediated cellular cytotoxicity.

Claim 205 (Currently amended). The ~~The~~ method of claim 203, wherein said antibody has increased Fc receptor binding affinity.

Claim 206 (Previously presented). A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising:

(a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides;

(b) glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltranferase;

(c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and

(d) isolating said recombinant antibody;

wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein the majority of the N-linked oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are bisected.

Claim 207 (Previously presented). The method of claim 206, wherein said antibody has increased Fc-mediated cellular cytotoxicity.

Claim 208 (Currently amended). The ~~The~~ method of claim 206, wherein said antibody has increased Fc receptor binding affinity.

Claim 209 (Previously presented). A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising:

(a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides;

(b) glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltranferase;

(c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and

(d) isolating said recombinant antibody;

wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein the majority of the N-linked oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are nonfucosylated.

Claim 210 (Previously presented). The method of claim 209, wherein said antibody has increased Fc-mediated cellular cytotoxicity.

Claim 211 (Previously presented). The method of claim 209, wherein said antibody has increased Fc receptor binding affinity.

Claim 212 (Previously presented). The method of claim 210 or claim 211, wherein the majority of the N-linked oligosaccharides in said Fc region of said antibody produced by said glycoengineered host cell are bisected, nonfucosylated.

Claim 213 (Previously presented). A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising:

(a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides;

(b) glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltranferase;

(c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and

(d) isolating said recombinant antibody;

wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein at least 45% of the oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are complex structures.

Claim 214 (Previously presented). The method of claim 213, wherein said antibody has increased Fc-mediated cellular cytotoxicity.

Claim 215 (Previously presented). The method of claim 213, wherein said antibody has increased Fc receptor binding affinity.

Claim 216 (Previously presented). The method of any one of claims 168, 169, 171, 172, 189, 190, 191, 197, 201, 202, 203, 206, 209, or 213, wherein said host cell is selected from the group consisting of an engineered CHO cell, an engineered BHK cell, an engineered NS0 cell, and an engineered SP2/0 cell.

Claim 217 (Previously presented). The method of claim 216, wherein said host cell is an engineered CHO cell.

Claim 218 (Previously presented). The method of any one of claims 167, 170, 188, or 197, wherein said recombinant antibody is a chimeric antibody.

Claim 219 (Previously presented). The method of any one of claims 167, 170, 188, or 197, wherein said recombinant antibody is a humanized antibody.

Claim 220 (Previously presented). The method of any one of claims 167, 170, 188, or 197, wherein said recombinant antibody is an antibody fragment that contains a Fc region.

Claim 221 (Previously presented). The method of any one of claims 167, 170, 188, or 197, wherein said recombinant antibody is a fusion protein that includes an Fc region of an immunoglobulin.

Claim 222 (Previously presented). The method of any one of claims 167, 170, 188, or 197, wherein said antibody is a therapeutic antibody.

Claim 223 (Previously presented). The method of any one of claims 167, 170, 188, or 197, wherein said antibody selectively binds to an antigen expressed by a cancer cell.

Claim 224 (Previously presented). The method of claim 223, wherein said antigen is differentially expressed by said cancer cell.

Claim 225 (Previously presented). The method of any one of claims 167, 170, 188, or 197, wherein said antibody is a monoclonal antibody.

Claim 226 (Previously presented). The method of any one of claims 168, 169, 171, 172, 189, 190, 191, 197, 201, 202, 203, 206, 209, or 213, wherein said antibody is

selected from the group consisting of: an anti-CD20 antibody, an anti-human neuroblastoma antibody, an anti-human renal cell carcinoma antibody, an anti-HER2 antibody, an anti-human colon, lung, and breast carcinoma antibody, an anti-human 17-1A antigen antibody, a humanized anti-human colorectal tumor antibody, an anti-human melanoma antibody, and an anti-human squamous-cell carcinoma antibody.

Claim 227 (Previously presented). The method of claim 226, wherein said antibody is an anti-CD20 antibody.

Claim 228 (Previously presented). The method of any of claims 168, 169, 171, 172, 189, 190, 191, 197, 201, 202, 203, 206, 209, or 213, wherein said at least one glycoprotein-modifying glycosyl transferase is mammalian.

Claim 229 (Previously presented). The method of claim 228, wherein said at least one glycoprotein-modifying glycosyl transferase is human.

Claim 230 (Canceled).

Claim 231 (Previously presented). The method of any one of claims 167, 170, 188, or 197, wherein said IgG Fc region containing N-linked oligosaccharides comprises an entire IgG Fc region.

Claim 232 (Previously presented). The method of any one of claims 167, 170, 188, or 197, wherein said IgG Fc region containing N-linked oligosaccharides comprises an IgG fragment.

Claim 233 (Previously presented) The method of claim 232, wherein said IgG fragment comprises a CH2 domain.

Claim 234 (Previously presented). The method of any one of claims 168, 169, 171, 172, 185, 186, 189, 190, 192, 193, 198, 199, 201, 202, 204, 205, 207, 208, 210, 211,

214 or 215, wherein said recombinant antibody is expressed from one or more expression vectors introduced into said host cell after said glycoengineering.